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STUDIES ON LUNG TUMOR 1
A STATISTICAL STUDY OF AUTOPSY CASES OF TUMORS AND THEIR LUNG METASTASIS

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As proof of the rapid increase of tumor cases in recent years, the Ministry of Welfare reported last year that death rate from tumors had taken the first rank with that of cerebral hemorrhage and thrombosis in death rate in Japan. It might possibly be inferred the reason for the increase of tumor cases is relative, depending on the decrease of death rate due to serious bacterial infections, especially tuberculosis, and the prolongation of human life.

However, the remarkable increase of lung cancers is of special significance in clinic of chest disease. Many such tumor cases have also been examined at the clinic of Tuberculosis Research Institute of Kyoto University. However, it is also necessary for investigation of lung tumors to deal not only with patients suffering from primary lesions but with metastatic lung tumors from resected materials. From this point of view, pathologic specimens in the depertment of Pathology of Kyoto University were reexamined to statistically clarify the incidence of tumors in various organs and the metastases from those to the lung.

MATERIALS AND METHODS;

The records of 8915 autopsy cases that those which had been examined at the Department of Pathology of Kyoto University since April 1901, were reviewed. Thirty additional cases were omitted from the total death rate because of inadequate records.

The rate of incidence of tumors in various organs and the rate of metastasis to the lung from those tumors were determined by checking the cases recorded from 1946 until the present time. At the same time microscopic examinations of all specimens on file were performed in addition to the checking of the records.

RESULTS;

a) Statistics of diseases by cause of death.

As to the cause of death, almost all of tuberculosis cases were pulmonary and miliary. Extrapulmonary tuberculosis was seen in a few cases. The total of tumor cases includes some deaths from post-operative complications.

The vast majority of pulmonary cancers were primary lung cancers including a few primary cases of sarcoma and fibroma. Among mediastinal and pleural tumors, those thought to be of primary lung origin were added to the pulmonary tumors.

The results, divided into 5 year groups, are shown in Table 1 and Fig. 1.

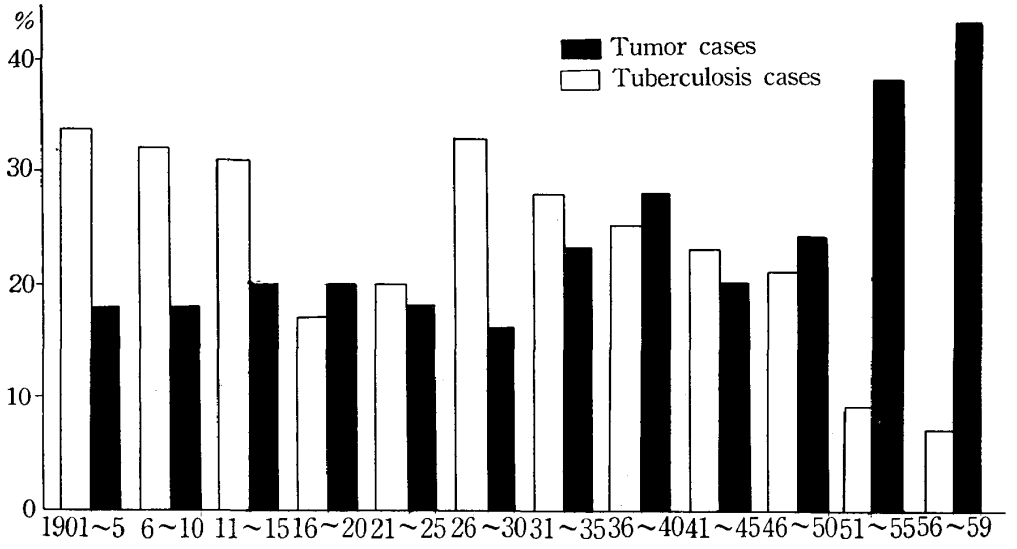

Fig. 1. Percentages of tuberculosis and tumor cases in the all autopsy cases at the Department of Pathology of Kyoto Univ.

Table 1. Statistics of autopsy cases at the Department of Pathology of Kyoto Univ.

Year	1901 ~5	1906 ~10	1911 ~15	1916 ~20	1921 ~25	1926 ~30	1931 ~35	1936 ~40	1941 ~45	1946 ~50	1951 ~55	1956 ~60
Autopsy cases on file	796	945	1045	906	624	759	681	428	468	426	573	894
Tuberculosis	271	312	322	162	128	245	187	101	95	90	50	61
Percentage of all cases	34	32	31	17	20	33	28	25	23	21	9	7
Tumor	143	177	248	185	108	123	160	121	82	106	222	390
Percentage of all cases	18	18	20	20	18	16	23	28	20	24	38	43
Lung tumor	3	2	7	3	2	2	0	1	4	3	17	41
Percentage of all tumor cases	2	1	2	1	1	2	0	1	5	3	8	11

The death rate of tuberculosis was the highest from 1901 to 1905 (34%), and then decreased progressively. The rapid increase found in the period from 1920 to 1930 was caused by the incaease of autopsy cases from a newly established Utano National Sanatorium. Apparent decrease of death from tuberculosis since 1951 was thought to be the result of chemotherapy. In contrast with tuberculosis, the death rate due to neoplasm increased year after year. But the rapid increase from 1951

was rather suprising, and in the last five years since 1955 alone the number of deaths from neoplasms reached to 40~50% of the total death rate. It may be worth mentioning of the increase of pulmonary cancer. During the period from 1901 to 1940, primary pulmonary cancers were 1~2% of all tumors, and after that increased rapidly to 11% in the last five years. In 1959, the number of pulmonary tumor cases surpassed those due to tuberculosis. Table 2 and Fig. 2 compare the death of tuberculosis with that of neoplasm since 1945.

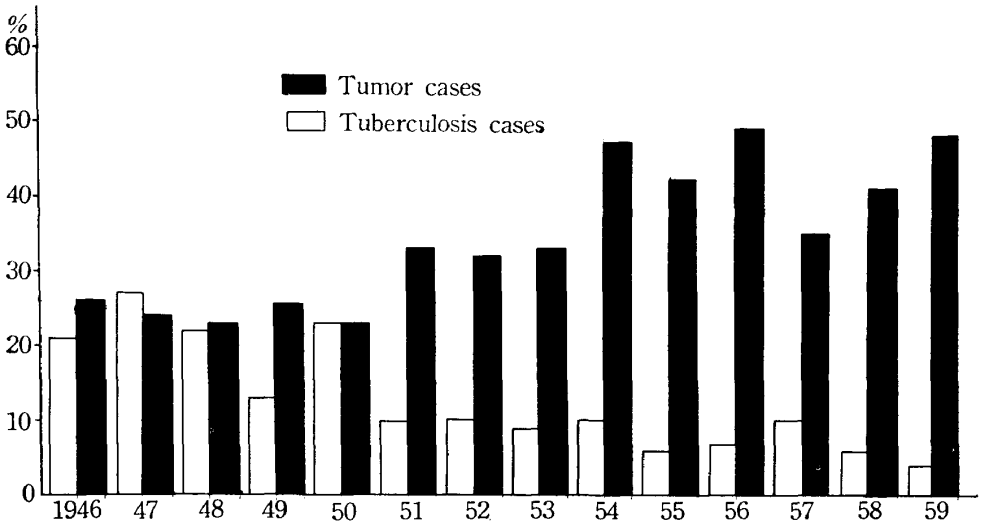

Fig. 2. Percentages of tuberculosis and tumor cases in autopsy cases at the Department of Pathology of Kyoto Univ. at the latest fourteen years

Table 2. Tuberculosis and tumor cases observed in autopsy cases at the Department of Pathology of Kyoto Univ. at the latest fourteen years

Year	1946	47	48	49	50	51	52	53	54	55	56	57	58	59	Total
Autopsy case on file	85	92	73	90	86	79	100	132	118	144	187	252	228	227	1893
Tuberculosis	18	24	16	12	20	7	10	12	12	9	13	24	14	10	200
Percentage of all cases	21	26	22	13	23	9	10	9	10	6	7	10	6	4	10
Tumor	22	22	17	23	22	27	32	43	58	62	91	88	102	109	718
Percentage of all cases	26	24	23	26	24	33	32	33	48	42	49	35	46	48	38
Lung tumor	0	0	0	2	1	2	5	3	3	4	8	7	9	15	59
Percentage of tumor cases	0	0	0	7	5	8	16	7	5	7	9	8	9	14	8

b) Investigations with reference to the primary organs of neoplasms.

Tumors were classified into two large categories, that is, benign and malignant. Leukemia and sarcoma were separated from other malignant neoplasms

into special classes. Tumors originating in the brain or nervous system were omitted from the present study because of their special nature and difficulty in classification. In addition, all tumors listed in the tables as neoplasms from the sensory organs were almost entire from the skin. Classification is shown in Table 3.

Table 3. Classification of tumor cases according to the organs from which the tumor originated

Organ \ Year	1946	47	48	49	50	51	52	53	54	55	56	57	58	59	Total
Sensory organs			1							1		1			3
Internal secretion organs		2			2				1	1	2	3	3	4	18
Digetative organs	5	9	2	10	5	12	9	10	16	15	28	19	29	29	198
Liver and pancreas	4		1	4	3	3	2	5	5	5	18	10	18	16	94
Respiratory organs				3	1	2	6	4	4	4	8	11	9	15	67
Urinar organs (♂)						1	2	1	3	2	3	4	4	4	24
Genital organs (♀)	1		1		1				1	1		1	2	3	11
〃 〃	5	1	2	2	4	2	1	7	3	6	6	14	6	7	66
Others	2	3	4	1	1	2	4	1	2	3	2	6	7	4	42
Total of Cancers	17	15	11	20	17	22	24	28	35	38	67	69	78	82	523
Brain	1	1	1	1			2	3	4	8	7	3	3	3	37
Sarcoma	2	1	3	1		3	1	3	7	6	8	4	9	11	59
Leukemia	2	5	2	1	3	1	5	9	10	9	8	10	8	9	82
Benign tumor					2	1			2	1	1	2	3	4	16
Total	22	22	17	23	22	27	32	43	58	62	91	88	101	109	717

As a characteristic of neoplasms in Japan, it is shown also in this study that cancer from gastrointestinal organs is the most frequent of all cancers. Liver, pancreas and genital organs followed in descending order. Cancer of respiratory organs is the fifth, but has increased since 1949 and it is of interest that this increase shows a sharp rise since 1956. Genitourinary cancer also has increased recently.

As for cancers in the other organs, neither apparent increase nor decrease is noted as in the case with sarcoma and leukemia.

c) Investigation with reference to the metastasis of neoplasm to the lung.

It has been shown in Table 4 that in a total of 504 cancer cases, metastasis to lung occurred in 194 cases. This is 38% of all cancer cases. Besides, it is found that the metastasis of sarcoma to the lung is 48% of all sarcoma cases and is likely a little more frequent than that of carcinoma. When all cancers are divided according to anatomical systems, it is shown that the rate of metastasis is the highest in the genitourinary system and the lowest in the digestive

Table 4. Lung metastasis of tumors (1946~1959)

Organ	Number of tumor cases	Cases of lung metastasis	Percentage %	Number of hilar lymph node metastasis	Percentage %
Sensory organs	3	2	(67)	1	(33)
Internal secretory organs	18	7	39	4	22
Digestive organs	192	63	33	42	22
Liver and pancreas	92	38	41	18	20
Respiratory organs	64	25	39	35	55
Urinar organs (♂)	24	11	46	4	17
Genital organs (♀)	11	5	45	1	9
" "	61	29	48	11	18
Others	39	14	36	9	23
Total	504	194	38	125	23
Sarcoma	50	24	48	11	22
Total	554	218	39	136	25

system. The difference between the rate of metastasis from these two system is not so great, but marked differences were found when the tumors were classified by organ or tissue in which the tumor originated.

Table 5 shows the rate of metastasis to the lung from each organ. It seems that metastasis of cancer from the maxilla, breast, kidney and ovary are of relatively high frequency and those from rectum, urinary bladder, pancreas and stomach occur less frequently. The rate of metastasis of hepatic cancer is about 50%, and this value is almost the same as the rate of metastasis of hepatoma. It is of interest that the rate of metastasis of chorioepithelioma is very high, 12 out of 13 cases, showing almost 100%, whereas the rate of metastatic cancer of the uterus is rather low, showing 25%. Metastases from the brain is very rare, and its rate is only 5%.

Table 5 also shows the classification according to Welther's type[1]. This shows the type of hematogeneous spread of tumor metastases; type II being called the hepatic type, type III, the large circulatory type, and type IV, the portal type. The rate of both type II and III is 50% and that of type IV is only 32%. This seems to indicate that the cancer cells are filtered and removed from the blood stream in the liver and thus metastase to the lung is prevented. Metastasis to the hilar lymph nodes of the lung is shown in Table 4. Metastasis to the hilar lymph nodes from each organ is only 9~23%, except for the respiratory organ. It is clear that metastasis to the hilar nodes is less than that to the lung tissue. As for the lung tumor metastasis to the hilar lymph nodes is very frequent, showing a rate of 5%, and this rate is two times as high as the rate of metastasis to the other lung. The rate of metastasis of sarcomas to the hilar lymph nodes is 22% and is almost equal to the rate of cancer metastasis.

Table 5. Lung metastasis of tumors according to Welther's classification

Welther's type	Organ	Cases examined	Case of metastasis		Percentage
II	Liver	26	13		50
	Liver (Hepatoma)	20	10		50
	Gall-duct (Intrahepatic)	7	3		43
	Total	53	26		50
III	Maxilla	11	9		81
	Parotis	2	2		(100)
	Tongue	3	0		0
	Thyroid	5	4		80
	Thymus	2		2	
	Pharynx	5	3		60
	Larynx	3	2		67
	Breast	9	7		78
	Oesophagus	16	6		37
	Rectum	8	2		25
	Kidney	7	6		86
	Suprarenal	9	4		44
	Bladder	15	4		26
	Uterus	35	9		25
	Uterus (Chorioepithel)	13	12	1	100
	Ovary	9	6		67
	Prostata	8	3		37
	Penis	1	0		0
	Skin	3	1		33
	Total	164	80	3	50
IV	Pancreas	23	7		30
	Stomach	163	53	3	33
	Gall-duct (Extrahepatic)	15	3		20
	Colon	7	4		57
	Peritoneal	8	3		38
	Gallbladder	3	0		0
	Total	219	70	3	32
	Brain	38	2		5
	Hypophysis	3	0		0
	Total	41	2		7

DISCUSSION AND SUMMARY;

Although the number of autopsies performed at the Department of Pathology, Kyoto University, are rather small in comparison with the number done in European and American labolatories, it seems that the number of 8915 is not

too small to show the variation of important diseases in Japan throughout these 60 years as revealed by autopsy findings.

The present investigations dealing with tuberculosis and neoplasm show marked changes in occurrence and death rates. In the past 10 years, death from tuberculosis rapidly decreased on account for the chemotherapy. Contrarily death from neoplasm increased year after year, and rapidly increased in the past ten years. Especially the recent increase of the pulmonary cancer was remarkable, and the death of cancer became more frequent than that of tuberculosis in autopsy cases.

Among deaths from neoplasm during the past ten years, death of sarcoma and leukemia totaled 512 cases. The death rate of cancer is about 3~4 times as much as that of sarcoma.

No remarkable difference is seen when the rates of metastasis to the lung are classified according to organ systems. When classified, however, according to changes of spesific organs or tissues, the rate of metastasis is quite different. When organs are classified according to Welther into the hepatic type, the large circulatory type and the portal type, the metastasis to the lung from the former two types are certainly less than the third one.

In the data of Maehara (1959)[2] which was obtained by histological investigation of 134 tumor cases classified according to the Welther's type, the frequency of lung metastasis of these tumors is the highest in the large circulatory type (62.2%), the second in the portal type (52.8%), and the lowest in the hepatic type (47.0%). It must be considered that the disagreement of this data with present writer's data shows the deficiency of importance of the transport way of tumor cells. The principle of Welther's metastatic type was excluded from the data in which the tumor types were listed separately from types of tumors originating in the same organ.

Lung metastasis of tumors results from direct extension and hematogeneous and lymphogeneous spread. Metastasis by the bronchogeneous route is most frequently observed in the extension of lung cancer to another part of the same lung and is not important in the lung metastasis from extrapulmonary tumors. Direct extension need not be included in this statistics of lung metastasis because of the rare occurrence of mediastinal and pleural tumors. Lymphogeneous (especially retrogressive) metastasis have been considered the main route of implantation of tumor cells because of the high percentage of metastasis to hilar lymph nodes. The presence of cancerous lymphangitis was again shown in the Kuwahara's data (1952)[3] as in the old report of Recklinghausen (1885)[4]. But as shown in the Table 4, the rates of metastasis of cancer and sarcoma to hilar lymph nodes are almost the same (22 and 23%) and these are far less than the percentage of lung metastasis. This may refute the hypothesis that metastasis to the lung mainly occurs through the lymph pathway instead of the blood canal.

There are quite a few reports concerning the rate of metastasis to the lung. Schmidt (1904)[5] stated that the occurrence of lung metastasis was 68.3% of all autopsy cases on patients who died of neoplasms. Later the rate of lung metastasis was reported to be 28.6% by the research of Katain (1922)[6], 57.3% by Deelman (1934)[7], 58.3% by Kost (1926)[8], 82.4% by Kawachino (1936)[9], 30.3% by Turner (1940)[10], 28.7% by Hubeny (1940)[11], 27.7% by Welther (1948)[1], 46.4% by Abrams (1950)[12], 47.5% by Kuwahara (1952)[3], 29% by Willis (1952)[13], 22% by Lee (1955)[14], and 64.2% by Maehara (1959)[2]. In the present writer's research, it is clear that 38% of all cancer cases exclusive of primary pulmonary tumors have some macroscopic or microscopic evidence of lung metastasis. These data reported by many authors are not uniform according to the materials and methods used. So it is difficult to attempt to show any correlation in common among these different data.

Additionally, as the percentages of lung metastasis of tumors vary as to whether primary foci are classified according to organ systems, organs, or types of neoplasms, it may not be significant to discuss universal rates of metastasis of neoplasms to the lung.

In conclusion, we believe that (1) the lung metastasis of cancer is only a little less than that of sarcoma, and (2) the fact that metastasis to the lung occurs much more frequently than those to the pulmonary hilar lymph nodes, may suggest that the majority of metastasis of cancer to the lung pass through the blood canal of the greater circuratory system. Histological findings supporting this hypothesis will be reported in detail in the subsequent papers.

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